

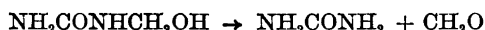
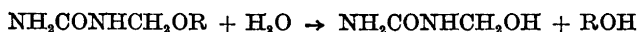
The Acid Hydrolysis of Alkoxymethyl Ureas

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The hydrolysis of alkoxymethyl ureas in acid solution has been investigated kinetically. The hydrolysis leads to the formation of methylol urea, which in turn will decompose to give formaldehyde and urea. The hydrolysis of the ether is a very fast reaction compared to the subsequent decomposition of the methylol compound. Values for the specific catalytic constant of H_3O^+ are given for some ethers with different ether-alkyl groups. Increased branching of the alkyl group increases the rate of hydrolysis. Ethers of methylol compounds of ordinary carboxylic acid amides are much more stable to acid hydrolysis than the ethers from methylolurea.

The alkyl ethers of methylolurea decompose in acid solution, leading to the liberation of free formaldehyde. From the kinetic experiments described below evidence is obtained that the reaction proceeds as follows:



In the first step the ether is hydrolysed giving methylolurea and alcohol. In the next step the methylolurea decomposes into urea and formaldehyde. The latter reaction is known to be acid catalysed¹. In the above scheme the first step, the ether hydrolysis, is a much faster reaction than the second. Formerly published results on the rate of the acid catalysed decomposition of alkoxy-methyl ureas², where the reaction has been followed by measurement of free formaldehyde formed, have, in fact, given the rate of the decomposition of methylolurea, the second step in the above scheme.

KINETIC INVESTIGATIONS

The kinetic investigations were performed in dilute water solutions (0.01—0.03 mole/l of ether). The pH was adjusted by use of acetic acid-acetate buffers or by addition of strong acid (HNO_3). In each experiment the ionic strength was adjusted to 0.2 by the addition of KNO_3 . To obtain the rate of

hydrolysis of the ether, step 1 in the above scheme, it is necessary to analyse samples from the reaction mixture for the sum of free formaldehyde and formaldehyde bound as methylol urea (= ether converted). This was achieved by transferring the samples into a solution containing excess KCN and enough NaOH to bring the pH to 13. Under these conditions the methylol urea is rapidly decomposed into urea and formaldehyde, and the latter reacts practically spontaneously with KCN. After 30 minutes at 25°C the excess KCN is titrated with $\text{Hg}(\text{NO}_3)_2$ ³.

Use of higher alkalinity to speed up the rate of decomposition of the methylol urea is not advisable as the hydrolysis of the ethers themselves then becomes more pronounced ⁴. Even at pH 13 the alkoxyethyl ureas will decompose to a small degree which has to be taken into consideration in calculating the rate constants as described later.

The hydrolysis of the ethers was followed up to about 75 % conversion. The rate of the reverse reaction of step 1 could be neglected under the experimental conditions.

The reaction was found to be of 1st order with regard to ether. Values for the specific catalytic constant of H_3O^+ for different ethers are given in Table 1.

The $[\text{H}_3\text{O}^+]$ values of the acetic acid-acetate solutions were calculated from the equation:

$$[\text{H}_3\text{O}^+] = K_a \cdot \frac{[\text{HA}]}{[\text{A}^-]} \cdot \frac{f_{\text{H}^+} \cdot f_{\text{A}^-}}{f_{\text{HA}}}$$

where f are activity coefficients. The value of the term $f_{\text{H}^+} \cdot f_{\text{A}^-} / f_{\text{HA}}$ was taken to be 0.60 at the given ionic strength = 0.2 ⁵.

Table 1. Specific catalytic constants of H_3O^+ for the hydrolysis of some alkoxyethyl ureas and methoxymethyl benzamide.

	$k_{\text{H}_3\text{O}^+}$ (l. mole ⁻¹ sec ⁻¹)	Temp. °C
$\text{NH}_2\text{CONHCH}_2\text{OCH}_3$	2.8	25
»	12.2	40
$\text{NH}_2\text{CONHCH}_2\text{OCH}_2\text{CH}_3$	3.9	25
$\text{NH}_2\text{CONHCH}_2\text{OCH}_2\text{CH}_2\text{CH}_3$	3.9	25
$\text{NH}_2\text{CONHCH}_2\text{OCH} \begin{smallmatrix} \text{CH}_3 \\ \diagup \\ \text{CH}_3 \end{smallmatrix}$	7.3	25
<hr/>		
$\text{C}_6\text{H}_5\text{CONHCH}_2\text{OCH}_3$	7.3×10^{-3}	40

As seen from the table the rate of hydrolysis increases with increased branching of the alkyl groups.

The rate constant of an ether of a methylol compound of an ordinary carboxylic amide, i. e. methoxymethyl benzamide is also included in the table for comparison. The rate constant of the latter is about 1 650 times lower than for the corresponding urea ether. The difference is due to the difference in activation energy, which was found to be 18.1 and 23.0 kcal/mole for methoxymethyl urea and methoxymethyl benzamide, respectively.

Any contribution of HAc to the rate observed in the acetic acid-acetate buffers could be neglected under the given experimental conditions; some results confirming this are given in Table 2.

Table 2. $[\text{Ac}^-] / [\text{HAc}] = 1.$

[HAc]	$\text{NH}_2\text{CONHCH}_2\text{OCH}_3$	$\text{C}_6\text{H}_5\text{CONHCH}_2\text{OCH}_3$
	Temp. 25°C $k \times 10^5 \text{ (sec}^{-1}\text{)}$	Temp. 40°C $k \times 10^7 \text{ (sec}^{-1}\text{)}$
0.2	8.2	2.1
0.06	8.1	2.1
0.02	8.1	2.1

Increasing the buffer concentration while keeping $[\text{H}_3\text{O}^+]$ constant does not influence the rate of hydrolysis. The rate constant observed in HAc—Ac buffers can therefore be taken as solely due to the effect of H_3O^+ .

Evidence for the proposed reaction scheme, *i. e.* that the monomethylol compound is initially formed by the hydrolysis, was obtained from kinetic experiments where the samples were separately analysed also for free formaldehyde. Free formaldehyde could be determined separately by reaction with KCN at pH~8. At this pH the methylol compounds are fairly stable while the KCN-formaldehyde reaction is completed⁶ within 5 min.

Results of these experiments with methoxymethyl urea and methoxymethyl benzamide are shown in Tables 3 and 4 where methylol compound + formaldehyde and free formaldehyde, as found experimentally, are given as % of initial amount of ether.

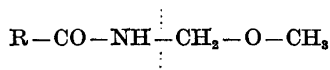
Table 3. Comparison between the amount of ether converted and free formaldehyde formed during the course of the reaction. HAc = 0.02 moles/l, B/A = 1. Temp. = 25°C.

Time (10^3 sec.)	Methoxymethyl urea % Ether converted (Methylol urea + CH_2O)	Free CH_2O %
1.8		1.2
3.9	27.1	2.0
7.2	44.8	3.2
14.4	69.3	4.0

Table 4. $[\text{HAc}] = 0.02 \text{ mole/l}$, B/A = 0.25. Temp. = 40°C.

Time (10^4 sec.)	Methoxymethyl benzamide % Ether converted (Methylol benzamide + CH_2O)	Free CH_2O %
8.28		1.6
17.37	13.0	2.6
28.71	21.0	3.1
54.72	35.5	3.8

It will be seen from Tables 3 and 4 that, even after conversion of a large percent of the ether, only very little free formaldehyde is present in the reaction mixture. This excludes the possibility that the ether is initially broken at the dotted line in



The hemiacetal thus formed would rapidly decompose to give free formaldehyde. Moreover, the methylol amide found could not have been formed from a recombination of free formaldehyde and urea. The equilibrium constant for this reaction is such that, with the dilute solutions used, most of the formaldehyde should exist in the free form. Furthermore, the rate constants for the reaction of amide and formaldehyde are much too low to allow any considerable recombination during the time of hydrolysis given in the tables.

REACTION MECHANISM

In spite of the fact that HAc showed no catalytic effect a mechanism which involves a general acid catalysis seems most probable. The effect of HAc may be difficult to detect because of the much greater effect of H_3O^+ in the pH range 4–5. Thus Dunn found a catalytic effect of piperidinium ion in the pH range 10.5–11.2 where a general acid effect should be more easily detected. The H_3O^+ catalysed reaction may therefore take place according to the following mechanism.

1. $\text{RCONHCH}_2\text{OR}' + \text{H}_3\text{O}^+ \xrightleftharpoons{\text{H}^+} \text{RCONHCH}_2\text{OR}' + \text{H}_2\text{O}$
2. $\text{RCONHCH}_2\text{OR}' + \text{H}_2\text{O} \xrightarrow[k_2]{\text{H}^+} \text{RCON}=\text{CH}_2 + \text{R}'\text{OH} + \text{H}_3\text{O}^+$
3. $\text{RCON}=\text{CH}_2 + \text{H}_2\text{O} \rightarrow \text{RCONHCH}_2\text{OH}$

In step 2, which is rate determining, alcohol is split off with the formation of an unstable Schiff's base which in step 3 adds water to give the methylol compound. The rate of the reaction catalysed by H_3O^+ will be given by:

$$= k_2 K_1 [\text{RCONHCH}_2\text{OR}'] [\text{H}_3\text{O}^+] [\text{H}_2\text{O}] (K_1 = [\text{RCONHCH}_2\text{OR}'] / [\text{RCONHCH}_2\text{OR}] [\text{H}_3\text{O}^+])$$

The great difference between the rate of hydrolysis of the urea and the benzamide ether is most probably explained by the effect of the group R on the value of k_2 . The formation of the double bound $\text{N}=\text{CH}_2$ with the simultaneous liberation of alcohol in step 2 involves an electron displacement from left to right. This displacement will most probably be hampered by the electron attracting C_6H_5 group and facilitated by the electron relasing NH_2 group.

An increased branching of the alkyl group will increase the basicity of the ether oxygen, and thus the value of K_1 in the rate equation. Apparently this effect more than outweighs the small counteracting effect which might be expected on the value of k_2 .

DISCUSSION

Recently Dunn² has published results from the acid decomposition of the methoxymethyl urea. However, he has determined the rate by measuring free formaldehyde liberated during the experiment. What really is measured therefore is the rate of reaction 2, *i. e.* the decomposition of methylolurea, which decomposes with a much slower rate than the ether hydrolysis in step 1. Thus Dunn finds a rate constant,

$$k_{\text{H}_2\text{O}} = 1 \times 10^{-3} \text{ (l} \cdot \text{sec}^{-1} \cdot \text{mole}^{-1}\text{) at } 25^\circ\text{C}$$

which is approximately the same as formerly given by de Jong and de Jonge for the decomposition of methylolurea. The value given in this paper is 2 800 times higher than the value given by Dunn.

The ethers were prepared according to procedures given by Kadowaki⁷ and Ugelstad and de Jonge⁴.

As mentioned above, the alkoxyethyl urea will also decompose to a small degree during the treatment with alkaline KCN solution used for determination of methylolurea and formaldehyde formed by the acid hydrolysis. This error is serious only with measurements taken at low conversions of the ether. It could be approximately corrected for as follows:

Let E_i = moles of ether in the sample taken from the reaction mixture at the start of the kinetic run ($t = 0$),
 F' = formaldehyde liberated from E_i moles of ether during the analysis,
 E_1 = the actual amount of undecomposed ether in the sample taken for analysis at a given time interval t_1 ,
 UF_1, F_1 = the corresponding values for methylolurea and free formaldehyde in the same sample,
 F = formaldehyde found by analysis of the sample taken at time t_1 ,
 Then the latter is approximately given by:

$$F = UF_1 + F_1 + F' \cdot E_1/E_i \quad (6)$$

A material balance for the ether gives:

$$E_i = E_1 + UF_1 + F_1 \quad (7)$$

Combination of eqns (6) and (7) gives the degree of conversion of ether at time t_1 :

$$\frac{E_i - E_1}{E_i} = \frac{F - F'}{E_i - F'}$$

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